AN INTERESTING CASE OF REFRACTORY IBD - HERMANSKY PUDLAK SYNDROME

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Abstract:
Hermansky Pudlak Syndrome is a rare autosomal recessive disorder which results in oculocutaneous albinism, bleeding problems due to functional platelet abnormality and systemic complications like IBD and pulmonary fibrosis. Presence of platelet functional abnormality leads to spontaneous rectal bleeding in IBD patients with HPS which makes scoring of disease activity difficult. Patients with HPS also have associated vWF deficiency. Bleeding manifestations in these patients can be successfully addressed with Desmopressin. We report a rare case of this syndrome with Crohns colitis which was successfully treated with Desmopressin and Azathioprine.

Keyword : IBD-Inflammatory bowel disease, HPS- Hermansky Pudlak Syndrome, vWF -Von Willi Brand Factor, CDAI - Crohns Disease Activity Index

INTRODUCTION:
Hermansky-Pudlak syndrome (HPS) is a complex syndrome with a triad of manifestations of oculocutaneous albinism, bleeding diathesis resulting from platelet dysfunction, and systemic complications associated with accumulation of ceroid lipofusion in reticuloendothelial tissues. Complications of the syndrome such as renal failure, cardiomyopathy, fatal pulmonary fibrosis and granulomatous colitis have been described. Colitis in HPS can be severe and has been reported to be poorly responsive to medical therapies including antibiotics, corticosteroids, sulfasalazine, mesalamine and azathioprine.

CASE REPORT
21 years old female, albino born of 2nd degree consanguinous marriage presented to our hospital in June 2013 with h/o loose stools admixed with blood and mucus since last 5 years with progressive worsening of symptoms since last 2 years. Patient also gave h/o episodic fresh rectal bleeding since last 5 years requiring blood transfusion atleast once in every 2 months since last 2yrs ,past history was significant with h/o easy bruising and recurrent epistaxis since childhood,. On examination, patient was emaciated, pale,
had pendular nystagmus & oculocutaneous albinism, patient had a low BMI of 12kg/m²

**MEDICAL HISTORY**

Patient was previously evaluated at various centers and had undergone multiple colonoscopic examination and biopsies, which were consistent with Crohn’s colitis limited to left colon. Patient had frequent relapses during first 3 years during which she was managed with mesalamine, oral steroids, azathioprine and symptomatic treatment. However, during the last 2 years there was no remission inspite of 3 doses of infliximab 5mg/kg at 0,2 and 6 weeks which was tried 1 year ago.

**INVESTIGATIONS**

Hb% - 3gms/dl, Total count and platelet count were normal, had elevated ESR of 60mm at 1sthr, Factor VIII assay showed 50% activity. BT, CT, APTT were within normal range, PT was prolonged by 1.5 secs. HRCT chest was done to rule out associated intestinal lung disease and was found to be normal. Colonoscopy showed inflammation with ulceration in sigmoid colon, descending colon and splenic flexure. Mucosal biopsy showed non caseating granulomas, lymphocytic infiltration of lamina propria, and crypt abscesses. There was no evidence of ceroid accumulation on histopathologic examination. Electron Microscopy showed deficiency of platelet dense bodies.

**TREATMENT**

Correction of anemia was done with 3 units of packed cells at admission. Patient was initiated on mesalamine at 2.4gms/day PO, oral prednisolone was started at 1mg/kg. Electron microscopy findings were available after 1 week and patient was started on Desmopressin nasal spray at 10mcg/spray BD in view of absence of platelet dense bodies on electron microscopy. Spontaneous rectal bleeding stopped after Desmopressin nasal spray. Oral prednisolone was tapered and stopped and patient was started on Azathioprine at 1mg/kg. During the 8 months of follow up there was no episode of rectal bleeding, no blood transfusion was required, patient was maintaining...
normal hemoglobin, had gained 8 kgs and had normal bowel habits with formed stools 1-2/day. However colonoscopy done in December 2013 still showed mild disease activity in Left Colon. Patients last follow up visit was in February 2014, and is lost to follow up since then.

Oculocutaneous Albinism

DISCUSSION

Schinella et al.² first reported granulomatous colitis in association with HPS in 1980. Colitis in HPS is unique in that the clinical features are suggestive of chronic ulcerative colitis and pathological features more closely similar to those of Crohn's disease³. It is unclear whether the granulomatous colitis in HPS is because of ceroid deposition or reflects the coexistence of Crohn's disease and HPS. Recent reports suggest that the colitis of HPS is simply a reaction to the tissue deposition of ceroid⁴. Yet, there are reported cases of HPS with gastrointestinal complications related to chronic granulomatous colitis, enterocolitis, ileitis, intestinal fistulization or granulomatous perianal disease³. These observations suggest that the colitis of HPS is due to the development of classical Crohn's disease. Therefore, it is possible that treatments known to be effective for Crohn's disease would be effective for HPS-associated enterocolitis. A review of reported cases reveals no consistent success with the standard medical treatment including sulfasalazine, mesalamine, corticosteroids and antibiotics, such as metronidazole and ciprofloxacin. In some cases surgical intervention is necessary, while subtotal colectomy or total proctocolectomy has been performed as a last resort. A review of the English language medical literature identified a total of 13 patients with HPS who required surgery due to lower GI bleeding, intractable colitis or perianal disease³. The granulomatous colitis associated with HPS usually manifests in the first and second decades and has been described as having a clinical
presentation similar to chronic ulcerative colitis and pathologic findings consistent with Crohn's disease. Colonoscopy commonly reveals multiple scattered superficial and deep ulcers, with pseudopolyps in some cases, from the rectum to cecum. Small bowel involvement is rare. Histologically, broad ulcers, which extend into the muscularis mucosa, brown granular pigmentation and non-necrotizing granulomas are seen. In patients with IBD, scoring the activity becomes difficult unless, treatment for rectal bleeding secondary to platelet dysfunction and vWF deficiency is addressed. In our patient though colonoscopic disease activity persisted, patient had significant improvement in quality of life, BMI increased from 12 to 15.6, CDAI decreased from 389 to 58 over 6 months. Control of spontaneous rectal bleeding as a result of administration of Desmopressin obviated the need for blood transfusion, and contributed to significant improvement in patients well being. Therefore, it is important to consider this syndrome in patients with albinism and IBD which helps not only to prognosticate but also has important implications in management.

REFERENCES:


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